

REMARKS

Claims 1-37 are pending in the application. Claims 1-23, 26-34, and 36-37 stand withdrawn pursuant to a restriction requirement. Favorable reconsideration in light of the amendments and the remarks which follow is respectfully requested.

I. The Amendments

Minor amendments are made to claim 24 to improve the wording thereof.

II. Rejection of Claims 24, 25, and 35 Under 35 U.S.C. § 103(a)

Claims 24, 25, and 35 stand rejected under 35 U.S.C. § 103(a) over Saulle et al (*Animal Sci.* 77, 3398-99 (1999)) in view of Lowe et al (*Nuc. Acid Res.*, 18, 1757-61 (1990)).

A. Applicants are NOT claiming a new or intended use for a known composition.

The claims are not presently rejected for novelty under any section of 35 U.S.C. § 102. The claims are rejected for obviousness under the provisions of 35 U.S.C. § 103(a) only. The Applicants' representative asserts that the claimed primer sequences are novel and such novelty has never been disputed by the USPTO.

The basis for the rejection, in the Examiner's words, is that "[i]t would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to combined the known nucleic acid sequences as taught by Saulle et al with a step of generate primers and designing primers as taught by Lowe et al." Office Action, page 3. That is, the basis for the rejection appears to be that Lowe et al will output multiple primers (a genus of primers), where selection of the claimed primers is obvious based on the output of that genus of primers. It is noted that is unknown if the actual claimed primers would be

among the output from the program of Lowe et al [add details about why not]. It is noted that the program of Lowe et al is almost 20 years and difficult to obtain. In any event, the claims are not rejected for reasons of novelty. Rather, since the rejection is only for obviousness, the only possible basis for the Examiner's rejection is that the claimed primers are structurally similar to, and therefore obvious, the primers potentially generated by program of Lowe et al.

In response to the comments made with the prior RCE submission the Examiner states:

Applicants' arguments were found unpersuasive. First, with regard to the claims as amended reciting utility of the primer pair to identify ruminants, Examiner notes that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re*

As stated, the claimed primers are novel as such has never been disputed by the USPTO. The claimed primers are structurally different from the prior art since the prior art does not disclose the claimed primers. Since Lowe et al only would generate primers that may be structurally similar to the claimed primers, structural similarity is not identity and, therefore, the sequence of the molecular structure of the claimed primers are structurally different from any primers that would be outputted by Lowe et al.

The Examiner states "the prior art teaches said [claimed] primers." Office Action, top of page 6. Again, the Examiner is reminded that the claims are only rejected for obviousness, and not for novelty. The cited documents clearly do not disclose the claimed primers. The claimed primers are specific, isolated chemical molecules with a discrete structure and molecular weight. Regardless of any whole gene sequence disclosed by Saulle et al, Saulle et al does not

disclose the claimed primers molecules with a molecular weight much lower molecular weight than the mitochondrial genome or the *ATPase8* gene as an independent, double-stranded DNA molecule. Further, the Lowe et al specifically teaches the output of primers having a different 3' end from the claimed primers. On page 1758, column 1, first paragraph of Lowe et al, Lowe et al teaches that "[a]ll primers should contain a GC-type sequence pair (i.e., either a CC, GG, GC, or CG) at their 3' end." The function of the algorithm is further described as "choosing sense primers with the GC-type sequence pair at their 3' ends." Lowe et al., page 1759, column 2, first full paragraph. That is, there is a structural difference between the claimed primers and any primer that would be outputted by the algorithm of Lowe et al. None of the steps of the algorithm of Lowe et al are optional.

The Board, in the prior appeal decision, suggests that the defect of Lowe et al may be cured, since "[w]hile some of the specific rules of Lowe might not apply. . . . one skilled in the art would have been [able] to identify primers within a larger sequence." Board Appeal Decision, page 7. That is, the Board is stating that the claimed primers are not actually disclosed as to be anticipated. The Board only asserts that one would be able to identify a sequence from Saulle et al. To restate in other words, the Board is only alleging structural similarity between the claimed primers and the sequence of Saulle et al rather than exact identity of chemical species. The claimed primers are not know compositions, but only ones that the Office and the Board allege would have been obvious to make by modifying allegedly disclosed larger DNA molecules. Applicants' representative does not agree with the Board's ultimate legal conclusions; however, it is clear that the claims are only rejected for obviousness, and therefore only case law relating to obviousness is applicable.

It is respectfully submitted that the Examiner's statements excerpted above and reference to *In re Casey* and *In re Mays* are only legally relevant to issues of anticipation under 35 U.S.C § 102. Such argument does not appear to have any relevance to the current obviousness rejection and does not serve to state a *prima facie* case of obviousness under 35 U.S.C § 103(a).

It is noted that on pages 6-9 of the current Office Action, the Examiner argues "a *prima facie* case of obviousness . . . based upon structural similarity." Office Action, page 6. However, any such theoretical showing of obviousness based on structural similarity can be rebutted by the applicant, as discussed below.

B. Disclosure of a genus does not necessarily make specific, undisclosed species conclusively obvious, and any assertion of a *prima facie* case for obvious based on structural similarity can be rebutted by the Applicant by showing unexpected properties of the claimed species.

It is well settled that "a species claim is not necessarily obvious in light of a prior art disclosure of a genus." *Eli Lilly & Co. v. Barr Indus., Inc.*, 222 F.3d 973, 986, 55 USPQ3d 1609, 1918 (Fed. Cir. 2000). Here, Saulle et al discloses a gene sequence, but does not disclose any specific primer species. Lowe et al is cited for an automated method to generate primer species. The specific primer species of the claims is synonymous with the situation of the status of species in light of an allegedly disclosed genus stated in *Eli Lilly* above. Disclosure of any genus that does not specifically enumerate the claimed primer sequences does not necessarily make the claimed primer sequences obvious.

Applicants' representative does not dispute that "evidence of nonobviousness is irrelevant for patentability purposes when an invention is anticipated under section 102." *In re Paulsen*, 30 F.3d 1475, 1482 n.11, 31 USPQ2d 1671, 1676 n.11 (Fed. Cir. 1994). However, the claims are only rejected for obviousness under 35 U.S.C. § 103(a); therefore, evidence of nonobviousness and unexpected properties of the claimed primers are relevant. The Federal Circuit has held that advantageous properties of a claimed species or sub-genus can always potentially rebut even a *prima facie* case of obviousness.

Under the *Papesch* doctrine [*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)] evidence of unobvious or **unexpected advantageous properties** may **rebut a prima facie** case of obviousness based on structural similarities. . . Such evidence may include data showing that a compound is unexpectedly superior in a property it shares with prior art compounds. . . . Evidence that a compound is unexpectedly superior in one of a spectrum of common properties . . . can be enough **to rebut a prima facie case of obviousness**.

In re Chupp, 816 F.2d 643, 646, 2 USPQ2d 1437 (Fed. Cir. 1987) (emphasis added).

The *Chupp* court ultimately held that an obviousness rejection to a claimed species of herbicide, structural similar to a prior art genus of herbicides, was rebutted by showing that the claimed species of herbicide was unexpectedly particularly effective against two types of weeds (quackgrass and yellow nutsedge). *Id.* at 647. The prior art genus of herbicides cited in the obviousness rejection in *Chupp* was known to have herbicide properties; however, a showing that the claimed, undisclosed species had an “unexpectedly superior” herbicide property was “sufficient to rebut the prima facie case of obviousness.” *Id.*

It follows that a rebuttal of obviousness is even stronger when it is shown that a specific species has properties not at all present in the disclosed members of a cited genus. Indeed, the *Papesch* decision cited by the *Chupp* court involved a claimed compound that possessed a new anti-inflammatory action not possessed at all by the cited structurally similar prior art compound. *Papesch*, 315 F.2d 381.

As discussed previously and summarized below with reference to the accompanying declaration, the claimed primers have an unexpected properties of species selection not shared with other primers targeted at the mitochondrial *ATPase8* gene. As discussed above, the claimed primers are not specifically disclosed in any cited art and the instant claims are only rejected for

obviousness, not novelty. Therefore, it is respectfully requested that the evidence of unexpected properties, contained in the accompanying declaration and within the Specification, be fully considered in judging the patentability of the claims, as required by the legal authority discussed above. Consideration of unexpected properties in a rejection under section 103 is required by Federal Circuit precedent. See *also*, MPEP § 2144.09(VII) (“A *prima facie* case of obviousness based on structural similarity is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties.”) (emphasis added).

C. The claimed primers have properties and functionality not shared by other primers targeted at the mitochondrial ATPase8 gene.

The claims are directed toward primer pairs that amplify ATPase8 gene sequences found in mitochondrial DNA originating from ruminants while having significantly reduced ability to amplify ATPase8 gene sequences originating from other animals. The Specification demonstrates the ruminant species discrimination abilities of the claimed primer pairs.

Figure 6 shows the discrimination functionality of the claimed ruminant-specific primers. It can be seen that the claimed primers (e.g., SEQ ID NOS: 3 & 4) can discriminate between cattle, sheep and goat (all ruminants) from non-ruminant, mammal species such as whale and pig, as well as other species. As shown in lanes 1-4 of Figure 6, the presence of ruminant DNA results in one PCR product having the weight of the ATPase8, rather than a more complex pattern that requires greater care to interpret. That is, the claimed primers have the property of not only discriminating between ruminant and non-ruminant species, but also provide a “yes/no”-type result via PCR.

The Specification also shows that other members of a genus of primer pairs targeted toward the *ATPase8* gene do not have the ability to amplify ruminant DNA to form a discrete PCR product while not amplifying non-ruminant DNA to form a discrete PCR product. For example, Figure 5 shows the results of

PCR performed with SEQ ID NOS: 1 & 2. As shown in Figure 5, primers having SEQ ID NOS: 1 & 2 have the property of amplifying the *ATPase8* gene.

However, SEQ ID NOS: 1 & 2 do not have the property of discriminating ruminant-derived DNA from DNA originating from other mammals. In Figure 5, SEQ ID NOS: 1 & 2 amplify DNA originating from ruminants (cattle, sheep, goat, and deer) equally well and form a product of the same weight as for DNA originating from non-ruminants (pig, horse, rabbit, and whale).

The accompanying declaration gives additional examples of primers that target the *ATPase8* gene but do not exhibit the ruminant-selective properties of the claimed primers. In pages 4 and 5 of the declaration, primers that detect some species of ruminant-derived DNAs but do not detect other species of ruminant-derived DNAs are described. To take case 6 shown in Appendix 3 as just one example, the ruminant goat is detected while the ruminants cow and sheep are not detected. This is not the same property as the claimed primers that reliably detect all ruminants. Further examples are specifically described in the declaration and/or are readily recognizable by study of the gels in Appendix 3 therein.

None of the multiple primers described in the Specification nor the accompanying declaration exhibit the described ruminant selective property, other than for the claimed primers. All of the described primers are competent to prime PCR from certain species, but none in a ruminant selective fashion other than the claimed primers. The Examiner states that "primers derived from said known sequence that identifies said species should obviously result in a number of primers that would identify only said species [that is, ruminants] and does not identify a non-ruminant species." Office Action, page 6. As described in reference to the enclosed declaration, the statement by the Examiner is manifestly untrue. There are no primers, other than the claimed primers, that have the described properties. The enclosed declaration fully meets the Applicants' burden in showing that the "number of primers" referred to by the Examiner do not exist.

That is, the claimed primers (e.g., SEQ ID NOS: 3 & 4) have a new, unexpected property not shared by other primers capable of amplifying the *ATPase8* gene via PCR. That property is the ability to amplify a discreet product from DNA originating from a ruminant species while not amplifying a discreet product from non-ruminant species. For example, primers of SEQ ID NOS: 1 & 2 do not have this property. In fact, no other primers targeted toward the mitochondrial *ATPase8* gene, other than the claimed primers, are known to have the described ruminant discrimination property. As the so-called “*Papesch* doctrine” established by the Federal Circuit states, evidence of unobvious or **unexpected advantageous properties** may **rebut a prima facie case of obviousness** based on structural similarities.” See, e.g., MPEP § 2144.09(VII). That is, even if the Examiner states a bare *prima facie* case obviousness, rebuttal evidence showing unexpected advantageous properties must be considered in rebuttal. Applicants’ representative submits that the demonstrated ability of the claimed primer pairs to discriminate ruminant DNA from non-ruminant is a sufficient new, unexpected and advantageous property to rebut any potential *prima facie* obviousness rejection. The Examiner is reminded that the claims are not rejected for anticipation, molecules having the precise structure of the claimed primers are not specifically shown in any document cited by the examiner, and the primers claimed are novel.

The “*Papesch* doctrine” is currently controlling law in the Federal Circuit and has been cited favorably in recent post *KSR Int’l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727 (2007), opinions and cited as controlling law in MPEP §§ 2141-2144. See, e.g., *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1086 (Fed. Cir. 2008) (“[T]he structure of the compound and its properties are inseparable considers in the obviousness determination.”) (citing *In re Papesch*, 315 F.2d at 391); *In re Sullivan*, 498 F.3d 1345, 1353 (Fed. Cir. 2007) (“The issue here is not whether a claim recites a new use, but whether the subject matter of the claim possesses an unexpected use. That unexpected property is relevant, and thus the declarations describing it should have been considered by the Board.”) (citing *In re Papesch*, 315 F.2d at 391, for stating “from the standpoint of patent law, a

compound and all of its properties are inseparable; they are one and the same thing"); see also MPEP § 2144.09(VII).

The recent decision of *In re Sullivan*, 498 F.3d 1354, is particularly relevant to the instant application. There, specific claimed Fab fragments (not claimed as a method) having antivenom properties were rejected by the Board for obviousness without the Board considering three declarations of the Applicant. The Federal Circuit vacated the Board's decision by stating "[w]hether the composition would have been obvious cannot be determined without considering evidence attempting to rebut the prima facie case," since "[t]here was no showing of unpatentability under § 102." *Id.* at 1351-52.

The accompanying declaration further sets forth additional advantageous properties of the claimed primers. The declaration describes the state of the art prior to the application of the Applicants. As shown in Figure 1 of the declaration, the only method for species identification available prior to the application of the Applicants was a PCR followed by restriction digestion of the PCR product. The result, as shown in Figure 1, is a complex electrophoretic pattern having several bands that must be compared to a standard or molecular weight markers in order to identify the species of origin. As explained in the declaration, the property of ruminant species determination allows for the advantageous properties of lower detection limit and less likelihood of misidentification.

D. Conclusion

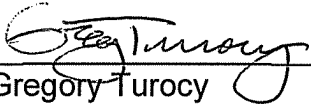
Applicants' representative does not agree with the Board's legal conclusion that a *prima facie* case of obviousness has been. A determination of a *prima facie* case of obviousness is controlled by the well-known *Graham* factors. See § 2141. Applicants' representative that regardless of the fulfillment or non-fulfillment of the *Graham* factors, controlling case law and MPEP § 2144.09(VII) requires the Office to consider rebuttal evidence that "the claimed compounds [i.e., the claimed primers] possess unexpectedly advantageous or superior properties."

The prior appeal to the Board only argues the non-existence of a *prima facie* case of obviousness. The Board in its prior decision does not seem to address a rebuttal of any such obviousness determination in light of the claimed primers possessing "unexpectedly advantageous or superior properties." More specifically, the evidence of "unexpectedly advantageous or superior properties" described in the attached declaration under 37 C.F.R. § 1.132 has not yet been considered. Applicant's representative submits that the described unexpected properties of the claimed primers are of sufficient quality to completely rebut an *prima facie* obviousness case that may be made under the *Graham* factors. Specifically, data in the Specification and the accompanying declaration show that no other primers, other than the claimed primers, directed toward the mitochondrial *ATPase8* gene show the ruminant species selective property in priming a PCR reaction. As such, the properties of ruminant species selectiveness qualifies as "unexpectedly advantageous or superior properties."

Therefore, it is respectfully requested that the rejection of claims 24, 25, and 35 under 35 U.S.C. § 103(a) be withdrawn.

In the event any fees are due in connection with this document, the Commissioner is authorized to charge those fees to Deposit Account No. 50-1063. Should the Examiner believe a telephone interview would be helpful to expedite favorable prosecution, the Examiner is invited to contact applicant's undersigned representative at the telephone number listed below.

Respectfully submitted,
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